US/04/33949

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Patent application No.: PA 2003 01514

Date of filing: 14 October 2003

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Titlel: A medical tubing for insertion into the vascular system of a living

IPC: -

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12 November 2004

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PATENT- OG VAREMÆRKESTYRELSEN

15661DK00

A MEDICAL TUBING FOR INSERTION INTO THE VASCULAR SYSTEM OF A LIVING

Technical field

The present invention relates to a method of producing a medical tubing for insertion into the vascular system of a living, in particular an intravascular stent or catheter. The invention also relates to such a medical tubing.

Background of the invention

Medical tubings, including stents and catehters, are often used in various diagnostic procedures and medical treatments. Fluid drugs may for example be delivered into the vascular system of a living by means of intravascular stents. Stents for implantation in the lumen of a body duct are mainly used in the treatment of blood vessels exhibiting stenosis. It is generally desired that medical tubings for insertion into the vascular system of a living meet certain physical requirements. For example, the medical tubings must be able to conform to an often tortuous passage to the treatment site while being sufficiently rigid to enable secure insertion. Furthermore, the surfaces of such medical tubings should be hydrophilic and have a low surface friction in order to facilitate introduction. The surfaces are often coated with nitric oxide in order to ensure that the surfaces are hydrophilic. Nitric oxide also reduces or prevents spasm once the medical tubing is in place. Medical tubings which are intended to release drugs once inserted into the vascular system of a living are usually covered or coated with appropriate pharmaceutical compounds. Expandable stents are often placed on an angioplasty balloon catheter which, once in place, is inflated in order to cause the stent to expand. Alternatively, stents may be made from a material which has a reovery capacity, so that the stents may automatically expand, once in place.

In the prior art, various medical tubings, including stents and catheters, as well as methods for their manufacture have been proposed. US patent No. 6,030,371 discloses a method for nonextrusion manufacturing of catheters that can be used to produce catheters. A polymer material in a particulate preform is applied in a layer over an outer surface of a core member. By applying the layer in a particulate preform, a composition of the polymer material can be varied continuously as it is being applied to provide a variable hardness over the length of the catheter. A fibrous reinforcement can be used having a constant or variable pitch and a constant or variable number of fibers and fiber types may be employed. US 6,030,371 further discloses the use of a plurality of mandrels placed side-by-side to form a multiple lumen tubing.

Various nictric oxide (NO) donor compounds, pharmaceutical compositions containing such nitric oxide donor compounds and polymeric compositions capable of releasing nitric oxide have also been proposed in the prior art. US patent No. 5,691,423 discloses a polymeric composition capable of releasing nitric oxide, and US 5,962,520 is concerned with a polymer capable of carrying and releasing a pharmaceutical compound. US 5,958,427 is directed to nitric oxide donor compounds and to pharmaceutical compositions for pulmonary hypertension and other indications, and US 6,147,068 discloses a composition of amine that was reacted with nitric oxide for delivering nitric oxide.

Summary of the invention

It is an object of the present invention to provide a new method for producing a medical tubing for insertion into the vascular system of a living.

In a first aspect, the invention provides a method of producing a medical tubing for insertion into the vascular system of a living, the method comprising the step of forming at least a portion of the medical tubing by spinning of nanofibers, preferably electrospinning of such nanofibers, which consolidate to form the medical tubing, or at least said portion thereof. It has been found that such spinning of nanofibers may be more easily or accurately controlled than methods relying solely on spraying of polymers toward a core. This may ultimately confer the further advantage that medical tubings may be made with smaller diameters than hitherto. The present invention allows for the manufacture of tubings, in particular stents, with relatively low diameters which, in comparison to stents with larger diameters, facilitate introduction of medical tubings into the vascular system of a living and reduce side-effects which may occur as a consequence of the introduction of medical tubings. It has also been found that medical tubings produced by preferred embodiments of the method according to the invention have a low surface friction, and that medical tubings may be produced which are well-suited as reservoirs to drugs, i.e. medical tubings in which the electrospun portions thereof constitute reservoirs for holding drugs. The tubings disclosed herein may carry any appropriate drug, including but not limited to nitric oxide compositions and heparin.

Various polymer-based materials may form the nanofibers, including polymer solutions and polymer melts. Applicable polymers are: nylon, fluoropolymers, polyolefins, polyimides, and polyesters. Further, carbon may be used as a fiber-forming material.

The art of electrospinning of nanofibers has developed considerably in recent years. US patent No. 6,382,526 discloses a process and apparatus for the production of nanofibers, which process and apparatus are useful in the method according to the present invention, and US patent No. 6,520,425 discloses a nozzle for forming nanofibers. It should be

understood that the processes and apparatuses of the aforementioned US patents may be applicable in the method according to the present invention, but that the scope of protection is not restricted to those processes and apparatuses.

Typically, the diameter of the nanofibers is in the range of 2 to 4000 nanometers, preferably 2 to 3000 nanometers.

The tubing produced by the present invention may define a plurality of sections along its length. For example, the sections may have different properties, such as different hardness. Such different properties may be arrived at by employing different fiber-forming materials for different sections and/or by changing production parameters, such as voltage of electrodes in the electrospinning process, distance between high-voltage and low-voltage electrodes, rotational speed of the tubing (or of a core wire around which the tubing is manufactured), electrical field intensity, corona discharge initiation voltage or corona discharge current.

Brief description of the drawing

A preferred embodiment of the invention will now be further described with reference to the drawing, in which:

Fig. 1 shows a longitudinal of a tubular stent produced by a method according to the invention.

Detailed description of the drawing

Though the invention will now be further described with reference to the stent illustrated in Fig. 1, it will be appreciated that the below description is not limited to medical stents. Accordingly, any other medical tubing for the introduction into the vascular system of a living may be produced as described below.

In one embodiment, the nanofibers are spun onto an outer surface of a core member. The core member comprises a core wire (or mandrel) 100, a layer 102 of PTFE applied to an outer surface of the core wire, a coating 104 of a thermoplastic material applied to an outer surface of the PTFE layer 102, and at least one reinforcing wire 106 applied to an outer surface of the thermoplastic coating, with the filaments of electrospun nanofibers being provided as an outer layer, i.e. enclosing the reinforcing wire and the thermoplastic coating.

Preferably, the diameter of the guide wire is at least 0.1 mm, preferably in the range of 0.1 to 1.0 mm. The thermoplastic coating, which is preferably a coating of polyurethane (PU), preferably has a thickness of 5 µm to about 0.05 mm, preferably 0.01 mm ±20%. The reinforcing wire(s) preferably has/have a diameter of 5 µm to about 0.05 mm, preferably 0.01 mm ±20%.

There may be provided one single core wire or a plurality of core wires which may be arranged side-by-side and extend in parallel. In the case of a plurality of core wires, the tubing so produced is a so-called multiple lumen tubing, with the core member being constituted by the plurality of core wires, around which the nanofibers are spun, so that the nanofibers and optionally the PTFE layer, thermoplastic layer and reinforcing wire(s) enclose the plurality of core wires. A multiple lumen tubing is for example useful in connection with pressure measurements, for example for measuring a pressure drop across stenosis. One or more passages of a multiple lumen tubing may be used for transmitting light, for example light which may be emitted through blood, thereby facilitating diagnostic procedures.

As described above, a layer of PTFE may be applied to an outer surface of the core member. At least a portion of the surface of the layer of PTFE, such as the portion onto which the nanofibers and/or the thermoplastic coating are to be applied, may be modified for improved bonding of material to the outer surface of the PTFE layer. Preferably, such modifying comprises etching, which may for example result in a primed PTFE surface for covalent bonding or gluing. The layer of PTFE may be provided as a hose which is slipped over and co-extends with the core wire, or, in the case of a multiple lume tubing, the plurality of core wires.

A coating of a thermoplastic material, such as polyurethan (PU), may be provided to an outer surface of the core member, i.e. to an outer surface of the PTFE layer in case such a layer has been provided. Following the step of providing the layer of PTFE and/or the step of providing the thermoplastic coating, one or more reinforcing wires may be applied to an outer surface of the core member, i.e., in a preferred embodiment, to an outer surface of the polyurethane coating. The reinforcing wire(s) may consist of one or wires made from steel or/and wires made from yarn, such as carbon filament, which may be applied by winding. Alternatively, the reinforcing wire may be applied by spinning of nanofibers, preferably by electrospinning as described above. The electrospun reinforcing wire may be formed from carbon or polymer, including polymer solutions and polymer melts. Applicable polymers are: nylon, fluoropolymers, polyolefins, polyimides, and polyesters.

While forming the medical tubing, or at least while forming that portion of the medical tubing which is formed by electrospinning, the core member is preferably rotated, so as to evenly distribute the nanofibers around the outer surface of the core member.

In a preferred embodiment of the invention, nanofibers are applied to the outer surface of the core member at this stage, that is preferably to the outer surface of the thermoplastic coating which is optionally reinforced by the reinforcing wire(s). The electrospinning process is discussed in detail above.

A solvent may subsequently be applied to an outer surface of the core member, the outer surface being defined by the electrospun portion (or layer) of the tubing. The thermoplastic coating thereby at least partially dissolves in the solvent, so as to bond the reinforcing wire(s) thereto. The reinforcing wire(s) thereby become(s) embedded in the thermoplastic coating. It has been found that the step of providing the solvent results in a highly dense surface with a low surface friction, which is believed to be due to crumpling or shrinking of stretched molecules of electrospun nanofibers once the solvent is applied.

A stent graft may be produced by omitting the step of applying the solvent.

The core wire (or mandrel) is removed from the tubing following the step of applying the solvent or prior to the step of applying solvent but subsequent to the step of applying the filament of electrospun nanofibers.

CLAIMS

1. A method of producing a medical tubing for insertion into the vascular system of a living, the method comprising the step of forming at least a portion of the medical tubing by spinning of nanofibers.

2. A method according to claim 1, wherein the step of spinning comprises electrospinning.

3. A method according to claim 1 or 2, wherein the diameter of the nanofibers is in the range of 2 to 4000 nanometers.

4. A method according to any of the preceding claims, wherein the step of spinning comprises feeding a first fiber-forming material into a nozzle for forming nanofibers by using a pressurized gas stream, and ejecting the first fiber-forming material from an exit orifice of the nozzle in the form of a plurality of strands of said first fiber-forming material that solidify and form said nanofibers.

5. A method according to any of the preceding claims, wherein the nanofibers are made from a polymer.

6. A method according to any of the preceding claims, comprising:
- providing at least one core member;
- forming the medical tubing by spinning the nanofibers onto an outer surface of the core member.

7. A method according to claim 6, wherein the step of providing the core member comprises providing a guide wire or a mandrel.

8. A method according to any of the preceding claims, wherein the diameter of the guide wire or mandrel is at least 0.1 mm.

9. A method according to claim 8, wherein the diameter of the guide wire or mandrel is at most 1.0 mm.

10. A method according to claim 6, wherein the step of providing the core member comprises providing a bundle of elongated members, so as to provide a multiple lumen tubing.

11. A method according to any of claims 6-10, further comprising, prior to the step of spinning, providing a layer of PTFE to an outer surface of the core member.

12. A method according to claim 11, further comprising modifying at least a portion of a surface of the layer of PTFE.

13. A method according to claim 12, wherein the step of modifying comprises etching.

14. A method according to any of the preceding claims, further comprising, prior to the step of spinning, providing a coating of a thermoplastic material to an outer surface portion of the core member.

15. A method according to claim 14, wherein the thermoplastic material is provided to an outer surface of the modified layer of PTFE.

16. A method according to claim 14 or 15, wherein the thermoplastic material consists essentially of polyurethane.

17. A method according to any of claims 6-16, further comprising applying, prior to the step of spinning, at least one reinforcing wire to an outer surface portion of the core member.

18. A method according to claim 17, wherein the at least one reinforcing wire is applied to an outer surface portion of the coating of said thermoplastic material.

19. A method according to claim 17 or 18, wherein the at least one reinforcing wire is applied by winding.

20. A method according to claim 19, wherein the reinforcing wire is made essentially from steel wire or yarn, such as carbon filament.

21. A method according to claim 17 or 18, wherein the at least one reinforcing wire is applied by spinning of reinforcing nanofibers.

22. A method according to claim 21, wherein the step of spinning said reinforcing nanofibers comprises electrospinning.

23. A method according to claim 21 or 22, wherein the diameter of the reinforcing nanofibers is in the range of 2 to 4000 nanometers.

24. A method according to any of claims 21-23, wherein the step of spinning said reinforcing nanofibers comprises feeding a second fiber-forming material into a nozzle for forming nanofibers by using a pressurized gas stream, and ejecting the second fiber-forming material from an exit orifice of the nozzle in the form of a plurality of strands of said second fiber-forming material that solidify and form said nanofibers.

25. A method according to any claims 21-24, wherein the reinforcing nanofibers are made from a polymer.

26. A method according to any of claims 7-25, further comprising removing the core wire or mandrel following the step of spinning said nanofibers.

27. A method according to any of claims 6-26, further comprising continuously rotating the core member while forming the medical tubing by spinning.

28. A method according to any of claims 17-27, further comprising applying a solvent to said outer surface portion of the core member, so as to bond the at least one reinforcing wire to the outer surface portion.

29. A method according to any of the preceding claims, wherein the solvent is applied subsequent to the step of forming said portion of the medical tubing by spinning of nanofibers.

30. A method of producing a medical stent assembly comprising an intravascular tubular stent, the method comprising producing the stent by a method according to any of the preceding claims.

31. A method of producing a medical catheter assembly comprising an intravascular tubular catheter, the method comprising producing the catheter by a method according to any of the preceding claims.

32. A medical tubing for a medical device and adapted to be inserted into the vascular system of a living, at least a portion of the medical tubing being formed by spun nanofibers.

33. A medical tubing according to claim 32, wherein said portion is formed by elctrospun nanofibers.

34. A medical tubing according to claim 32 or 33, wherein the diameter of the nanofibers is in the range of 2 to 4000 nanometers.

35. A medical tubing according to any of claims 32-34, wherein the nanofibers are made from a polymer.

36. A medical tubing according to any of claims 32-35, the medical tubing enclosing a bundle of elongated members.

37. A medical tubing according to any of claims 32-36, wherein an inner layer of the medical tubing consists essentially of PTFE.

38. A medical tubing according to claim 37, wherein at least an outer surface portion of the PTFE layer has been modified.

39. A medical tubing method according to claim 38, wherein outer surface portion of the PTFE layer has been modified by etching.

40. A medical tubing according to any of claims 32-39, wherein a coating of a thermoplastic material is provided to an outer surface portion of the PTFE layer.

41. A medical tubing according to claim 40, wherein the thermoplastic material is provided to an outer surface of the modified layer of PTFE.

42. A medical tubing according to claim 40 or 41, wherein the thermoplastic material consists essentially of polyurethane.

43. A medical tubing according to any of claims 40-42, wherein at least one reinforcing wire is applied to an outer surface portion of the coating of thermoplastic material.

44. A medical tubing according to claim 43, wherein the at least one reinforcing wire is made essentially from steel wire or yarn, such as carbon filament.

45. A medical tubing according to claim 43 or 44, wherein the at least one reinforcing wire is wound around said coating of thermoplastic material.

46. A medical tubing according to claim 43, wherein the at least one reinforcing wire is applied by spinning of reinforcing nanofibers.

47. A medical tubing according to claim 46, wherein the at least one reinforcing wire is applied by electrospinning of the reinforcing nanofibers.

48. A medical tubing according to claim 47, wherein the diameter of the reinforcing nanofibers is in the range of 2 to 4000 nanometers.

49. A medical tubing according to any of claims 46-49, wherein the reinforcing nanofibers are made from a polymer.

50. A stent assembly comprising an intravascular tubular stent, the tubular stent comprising a medical tubing according to any of claims 32-49.

51. A stent assembly according to claim 50, wherein the portion of the medical tubing which has been formed by spinning of nanofibers constitutes a reservoir to hold at least one drug.

52. A stent assembly according to claim 51, wherein said at least one drug is liquid-based.

53. A stent assembly according to claim 51 or 52, wherein said at least one drug comprises nitric oxide.

54. An intravascular medical catheter comprising a medical tubing according to any of claims 32-49.

ABSTRACT

A method of producing a medical tubing, such as a stent or catheter, for insertion into the vascular system of a living comprises the step of forming at least a portion of the medical tubing by electrospinning of nanofibers, which consolidate to form the medical tubing, or at least said portion thereof. A PTFE layer is provided to a core wire or mandrel, onto which a PTFE layer is applied, a surface of which is modified by etching. A thermoplastic coating, such as a polyurethane (PU) coating is applied to the PTFE layer, and one or more reinforcing wires are wound or spun onto the coating. A filament of the electrospun nanofibers is then applied, and a solvent is used to embed the reinforcing wires in the coating. The filament of electrospun wires may be used as a reservoir to hold drugs, e.g. pharmaceutical components of nitric oxide (NO) and/or heparin. Multiple lumen tubings may be used for pressure measurements, e.g. across stenosis, and/or for transmitting light for diagnostic purposes.

(Fig. 1)

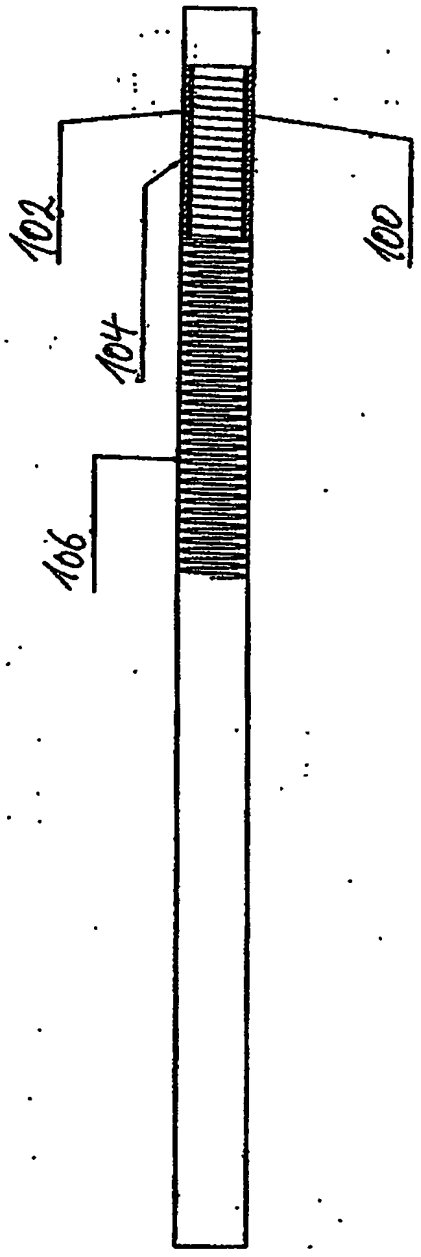

Fig. 1

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US04/033949

International filing date: 14 October 2004 (14.10.2004)

Document type: Certified copy of priority document

Document details: Country/Office: DK
Number: PA 2003 01514
Filing date: 14 October 2003 (14.10.2003)

Date of receipt at the International Bureau: 21 February 2005 (21.02.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)

World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse